**TECHNICAL APPENDIX**

# Intervention strategies to reduce the burden of non-communicable diseases in Mexico: cost effectiveness analysis

Joshua A Salomon, Natalie Carvalho, Cristina Gutiérrez-Delgado, Ricardo Orozco, Anna Mancuso, Daniel R Hogan, Diana Lee, Yuki Murakami, Lakshmi Sridharan, María Elena Medina-Mora, Eduardo González-Pier

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This appendix provides details on methods and assumptions used in modeling population health effects, costs and cost-effectiveness within each intervention cluster.

## Contents

## Depression

Analysis of the cost-effectiveness of depression in Mexico was contextualized from the WHO-CHOICE regional analysis for AMR-B.[1]

*Definition of interventions*

We considered 4 main interventions for the treatment of depression: (1) older anti-depressants in primary care; (2) newer anti-depressants in primary care; (3) brief psychotherapy in primary care; and (4) proactive case management.

Older anti-depressants refer to tricyclic anti-depressants (TCAs), while newer anti-depressants denote selective serotonin reuptake inhibitors (SSRIs). A *status quo* scenario reflects the combination of these interventions at current estimated coverage levels in Mexico. For all other analyzed strategies we defined the target coverage level to be 50%.

In addition to considering single interventions, we also evaluated the following intervention combinations: (1) older anti-depressants + psychotherapy at target coverage; (2) newer anti-depressants + psychotherapy at target coverage; (3) older anti-depressants + psychotherapy + proactive case management at target coverage; and (4) newer anti-depressant + psychotherapy + proactive case management at target coverage.

*Estimation of benefits*

We modeled depression using the standardized WHO-CHOICE outcomes model, distinguishing susceptibles (those not experiencing depressive episodes); depressive episodes; and deaths. Depressive episodes reflected various associated comorbidities, mainly dysthymia, panic disorder, alcohol abuse and drug abuse. To avoid double-counting in comorbid cases, we followed the Global Burden of Disease approach of counting the case in the condition with the higher disability weight and subtracting the case from the prevalence figure of the other condition.

Estimates of current incidence, prevalence, remission and case fatality were derived from regional estimates in the Global Burden of Disease (GBD) study, as used in the previous WHO-CHOICE analysis.[1] Prevalence by age and sex is reported in Table A1. Health-state valuations for relevant disease states were calculated by WHO-CHOICE using the Dutch disability weight for depression,[2] which remains the current standard used in the global burden of disease study due to its level of detail in capturing functional consequences of depression at different severity levels.

**Table A1: Prevalence of depressive episode by age and sex (rates per 1000 population)**

| Age group (years) | Prevalence, male | Prevalence, female |
|---|---|---|
| 0-4 | 0.0 | 0.0 |
| 5-14 | 11.0 | 11.0 |
| 15-29 | 18.0 | 32.0 |
| 30-44 | 25.0 | 43.0 |
| 45-59 | 23.0 | 40.0 |
| 60-69 | 19.3 | 33.0 |
| 70-79 | 7.8 | 13.4 |
| 80+ | 5.9 | 10.1 |

Intervention effectiveness was derived through review of clinical trials, drawing from the sources and assumptions used in the published WHO-CHOICE regional analysis[1] (Table A2). Estimates of efficacy were adjusted to account for treatment coverage, partial response, and patient adherence. Interventions were compared to the null scenario in which the remission rate was assumed to be 2.0 per person per year, corresponding to an average duration of 6 months.

**Table A2: Intervention effectiveness inputs for depression (Source: WHO-CHOICE regional analysis[1])**

| Intervention | Reduction in incidence (%) | Reduction in disability (%) | Remission rate (per person per year) |
|---|---|---|---|
| TCA | | 12.9 | 2.7 |
| SSRI | | 13.7 | 2.7 |
| Psychotherapy | | 14.5 | 2.5 |
| TCA + psychotherapy | | 16.1 | 2.7 |
| SSRI + psychotherapy | | 16.1 | 2.7 |
| Pro-active management | 28 | 17.7 | 2.8 |

*Estimation of costs*

Key categories of patient costs associated with delivering the interventions in this analysis included drugs, hospital bed days, hospital visits and outpatient visits.

Drug costs for antidepressants were obtained from the IMSS price list (Int $0.05 per daily dose of imipramine and $0.09 per daily dose of fluoxetine). Costs for inpatient and outpatient visits were estimated using standardized WHO-CHOICE unit costs for Mexico[3] (Annex Table). We maintained quantity assumptions from the published WHO-CHOICE regional analysis,[1] which were based on data from prospective studies and a multi-national Delphi consensus study[4-7] (Table A3).

**Table A3: Annual quantities of inpatient bed-days and outpatient visits for depression interventions (Source: WHO-CHOICE regional analysis[1])**

| Intervention | Hospital bed-days | Hospital visits | Outpatient visits |
|---|---|---|---|
| Combination of interventions at current coverage | 9.9 | 6.1 | 3.4 |
| Older anti-depressant drug in primary care at target coverage | 7.4 | 4.3 | 5.1 |
| Newer anti-depressant drug in primary care at target coverage | 7.4 | 4.3 | 5.1 |
| Brief psychotherapy in primary care at target coverage | 7.4 | 4.3 | 5.1 |
| Older anti-depressant + psychotherapy at target coverage | 7.4 | 4.3 | 5.1 |
| Newer anti-depressant + psychotherapy at target coverage | 7.4 | 4.3 | 5.1 |
| Older anti-depressant + psychotherapy + proactive case management at target coverage | 5.6 | 3.3 | 5.1 |
| Newer anti-depressant + psychotherapy + proactive case management at target coverage | 5.6 | 3.3 | 5.1 |

## Heavy alcohol use

Heavy alcohol use is defined as an average rate of consumption of more than 20g of pure alcohol daily for women and more than 40g daily for men. Analysis of the cost-effectiveness of alcohol use in Mexico was contextualized from the WHO-CHOICE regional analysis for AMR-B.[8]

*Definition of interventions*

We considered 5 main types of interventions for primary and secondary prevention of heavy alcohol use: (1) taxation at current levels; (2) taxation at a level 25% above current; (3) taxation at a level 50% above current; (4) random breath testing (RBT) of drivers; (5) reduced access to retail outlets (sales); (6) advertising ban on TV, radio and billboards; and (7) brief primary health care (PHC) advice.

Taxation aims to reduce incidence of heavy alcohol use. The impact of taxes on consumption is reflected in estimates of the price elasticity of demand for alcohol. Random breath testing aims to enforce drunk-driving laws and reduce fatal and non-fatal traffic injuries, both among hazardous drinkers and among other population groups. The 'reduced access' strategy aims to reduce sales of alcohol by restricting hours of operation for retail outlets (for example, by prohibiting sales of alcohol on Sundays). A comprehensive ban on alcohol advertising (TV, radio, bill-boards) aims to reduce incidence and alcohol-related harm. 'Brief advice' entails educational information sessions and psychological counseling delivered in a primary health care setting. This intervention aims to increase remission rates from heavy alcohol use and reduce disability associated with alcohol use.

Six combinations of the above interventions were also analyzed: (1) increased tax + scaled-up random breath-testing; (2) increased tax + advertising ban; (3) increased tax + brief advice; (4) increased tax + advertising ban + brief advice; (5) increased tax + brief advice + advertising ban + reduced access; (6) increased tax + brief advice + advertising ban + reduced access + scaled-up random breath-testing. Mass media and school-based educational and awareness interventions were not included in this analysis because they have been shown to have low efficacy.[9 10]

*Estimation of benefits*

We modeled heavy alcohol use using the standardized WHO-CHOICE outcomes model, distinguishing the following 3 states: (1) susceptible; (2) case (heavy alcohol use); and (3) death. Estimates of current incidence, prevalence and risks of mortality were obtained from the *Encuesta Nacional de Adicciones* 2002. Prevalence estimates (Table A4) reflect an adjustment upward by a factor of 1.72 to account for underreporting of alcohol consumption, based on total reported consumption compared to actual sales.

**Table A4: Prevalence of heavy alcohol use by age and sex (rates per 1000 population)**

| Age group (years) | Prevalence, male | Prevalence, female |
|---|---|---|
| 0-4 | 0.0 | 0.0 |
| 5-14 | 0.3 | 0.1 |
| 15-29 | 86.3 | 17.3 |
| 30-44 | 183.6 | 27.3 |
| 45-59 | 174.6 | 20.0 |
| 60-69 | 135.7 | 12.3 |
| 70-79 | 126.3 | 7.1 |
| 80+ | 125.5 | 7.1 |

Estimates of remission and case-fatality were derived from WHO's Comparative Risk Assessment analysis. Case fatality estimates were used to estimate relative risks of mortality: 2.5 for men and women 15-44 years of age; and 1.3 for men and 1.4 for women in older age groups.[8] The average remission rate was calculated using an average duration of 10.9 years to recovery, with an adjustment of +/- 20% for older and younger age groups, respectively.[8 11] Health-state valuations were derived from the weighted average of disability weights for each of two categories of drinkers, using the Dutch disability weight study,[2] following the standard in related work on the global burden of disease.

Intervention effectiveness was derived from a variety of prior studies, as reported in Table A5, adhering closely to the assumptions and sources used in the regional WHO-CHOICE analysis.[8] For taxation interventions, local estimates on the price elasticity of demand for alcoholic beverages, and information on the distribution of total consumption across specific beverage categories, were used to derive population-level effect estimates. The resulting population effect estimates were similar to those in the regional analysis.

**Table A5**: **Intervention effectiveness inputs for heavy alcohol use**

| Intervention | Effectiveness target | Effect estimate | Source |
|---|---|---|---|
| Taxation (current level) | Incidence of hazardous alcohol use | -10.1% | local data[a] |
| Taxation (current level + 25%) | Incidence of hazardous alcohol use | -11.6% | local data[a] |
| Taxation (current level + 50%) | Incidence of hazardous alcohol use | -12.7% | local data[a] |
| RBT of drivers | Incidence of fatal injuries | -18% | [12 13] |
| | Incidence of non-fatal injuries | -15% | [12 13] |
| Reduced access to retail outlets | Incidence of hazardous alcohol use | -2.5% | [14 15] |
| | Incidence of alcohol-related traffic fatalities | -3% | [14 15] |
| Advertising Ban | Incidence of hazardous alcohol use | -3% | [16-19] |
| Brief PHC advice | Population-level remission | 4.9 – 6.4% | [20 21] |
| | Average disability weight | -1.3% | [20 21] |

a. Local analyses of price elasticity of demand for specific types of alcoholic beverages undertaken based on data from Consultores Internacionales, combined with information on distribution of consumption across types.

In line with the general WHO-CHOICE guidelines, we excluded government revenues associated with increases in taxation, which can bring in financial gains in addition to health benefits.

*Estimation of costs*

Program costs for all interventions pertained to administration, training, enforcement, and educational and media costs. Estimates of resource quantities and prices were based on the previously published WHO-CHOICE regional analysis.[8]

Patient costs were applicable only for brief primary health care advice. Key categories of patient costs associated with delivering this intervention included primary health center visits, hospital outpatient visits and hospital bed days. Following the previous regional analysis, we assumed an average of 4 primary care visits over one year for the intervention itself, plus an average of 0.33 outpatient visits (based on 1.67 visits among 20% of the target population) and 0.25 inpatient days (based on 5 days among 5% of the population). Prices for inpatient and outpatient visits were estimated using standardized WHO-CHOICE unit costs for Mexico (Annex Table).

**Tobacco use**

Analysis of the cost-effectiveness of interventions for tobacco use in Mexico was contextualized from the WHO-CHOICE regional analysis for AMR-B.[22]

*Definition of interventions*

We considered 4 main types of interventions for prevention and reduction of tobacco use: (1) taxation of cigarettes at current levels of 60% of retail price (*status quo* scenario); (2) increased taxation of cigarettes, at 80% of retail; (3) clean indoor air law enforcement; (4) comprehensive advertisement ban; and (5) nicotine replacement therapy (NRT).

Taxation interventions were estimated to affect tobacco consumption via the price elasticity of demand for tobacco. Enforcement of clean indoor air laws has been shown to reduce both prevalence of smoking and average daily cigarette consumption among smokers. A comprehensive advertisement bad would prohibit all TV, radio and billboard ads for tobacco products. NRT was the only analyzed intervention directed at individuals rather than communities.

In addition to the single interventions, the following combination interventions were considered: (1) increased tax + advertising ban; (2) increased tax + clean indoor air laws; (3) increased tax + advertising ban + clean indoor air laws; and (4) increased tax + advertising ban + clean indoor air laws + NRT.

The effects of all interventions were modeled in terms of changes in ischemic heart disease (IHD), chronic obstructive pulmonary disease (COPD), cerebrovascular disease and lung cancer.

*Estimation of benefits*

We modeled tobacco use using the standardized WHO-CHOICE outcomes model, distinguishing the following 5 states: (1) susceptible; (2) disease X (IHD and COPD); (3) disease C (cerebrovascular disease); (4) disease XC; (5) dead.

Estimates of current incidence, prevalence and case-fatality were derived from the Global Burden of Disease analysis for Mexico (Table A6).

**Table A6: Epidemiologic estimates for analysis of tobacco interventions (rates per 1000 population)**

| | | Age group (years) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Disease indicator** | **Sex** | **0-4** | **5-14** | **15-29** | **30-44** | **45-59** | **60-69** | **70-79** | **80+** |
| IHD and COPD | | | | | | | | | |
| Incidence | Male | 0.0 | 0.1 | 0.2 | 1.0 | 4.7 | 10.9 | 14.6 | 26.8 |
| | Female | 0.0 | 0.1 | 0.2 | 0.9 | 2.6 | 6.3 | 9.9 | 17.7 |
| Prevalence | Male | 0.0 | 0.1 | 2.1 | 7.6 | 29.5 | 71.9 | 134.7 | 208.8 |
| | Female | 0.0 | 0.2 | 1.8 | 7.8 | 23.2 | 49.5 | 91.6 | 150.6 |
| Cerebrovascular disease | | | | | | | | | |
| Incidence | Male | 0.0 | 0.1 | 0.2 | 0.9 | 2.6 | 6.3 | 9.9 | 17.7 |
| | Female | 0.0 | 0.0 | 0.0 | 0.6 | 2.9 | 9.4 | 17.8 | 36.3 |
| Prevalence | Male | 0.0 | 0.0 | 0.0 | 1.3 | 9.7 | 33.9 | 53.8 | 55.0 |
| | Female | 0.0 | 0.0 | 0.0 | 1.3 | 8.8 | 26.4 | 41.4 | 46.0 |

Lung cancer mortality was added to background mortality so that intervention effects may also reflect reduced rates of lung cancer. Health-state valuations were derived from the GBD study.

The smoking impact ratio (SIR) was used as an indirect indicator of the accumulated hazard of smoking, in order to assess the effects of reductions in smoking on diseases of interest other than lung cancer. The

SIR is defined as population lung cancer mortality in excess of that observed in never-smokers, relative to excess lung cancer mortality for smokers. Lung cancer mortality rates of smokers were taken from the 2000 GBD study for AMR-B, while the American Cancer Society's 1990 Cancer Prevention Study (CPS –II) was used to obtain lung cancer mortality rates of non-smokers.[23] SIRs were computed from lung cancer mortality rates and compared to SIRs for the AMR-B region from the 2000 Global Comparative Risk Assessment (CRA) study. The CRA study was also used to obtain relative risks of IHD, COPD and cerebrovascular disease morbidity for smokers versus non-smokers, while relative risks of overall mortality were obtained from the CPS-II study.

Intervention effectiveness (Table A7) was modeled via reductions in tobacco consumption, using the SIR as a proxy for smoking prevalence. Revised SIRs were calculated for each intervention based on intervention efficacy and population coverage, with revised incidence and mortality rates calculated in turn from the new SIRs. For taxation interventions, which operate via price elasticities of demand for tobacco, price elasticities for tobacco products were estimated at -0.75 for ages 30+ and 25% higher for 15 to 30 year olds.[24] Illegal local consumption through smuggling was estimated to be 20% at the current taxation rate, with a 10% increase at higher tax rates.[24]

**Table A7: Intervention effectiveness inputs for tobacco use, expressed in terms of reduced consumption**

| Intervention | Effect | Source |
|---|---|---|
| Current taxation (60%), vs. null | | |
| 15-30 years | -71.5% | [24] (elasticity estimates) |
| 30+ years | -57.2% | [24] (elasticity estimates) |
| Increased taxation (80%), vs. current | | |
| 15-30 years | -79.6% | [24] (elasticity estimates) |
| 30+ years | -63.7% | [24] (elasticity estimates) |
| Clean indoor air laws | | |
| Males | -2.8% | [25] |
| Females | -0.9% | [25] |
| Comprehensive advertising ban | -5.0% | [26] |
| Nicotine replacement therapy | -3.1% | [24 27] |

The clean indoor air intervention analyzed in this model did not assess the associated benefits to non-smokers due to the reduction in exposure to environmental tobacco smoke, thus biasing downward the effectiveness of this intervention. Furthermore, we excluded government revenues associated with increases in taxation, which can bring in financial gains in addition to health benefits.

*Estimation of costs*

All interventions included program costs, estimated using the standard WHO-CHOICE framework. Strategies based on taxation and indoor air laws had basic administration costs (at the simplest level of complexity) and law enforcement costs. The advertising ban strategy had unique personnel costs at the central and state level. Only NRT included patient costs. The annual cost of nicotine gum was estimated at I$ 34 based on the unit price reported in the IMSS provider database. This estimate was based on a daily dose of 4mg and duration of 90 days.

## Cataracts

Analysis of the cost-effectiveness of cataract surgery in Mexico was contextualized from the WHO-CHOICE regional analysis for AMR-B.[28]

*Definition of interventions*

The only effective treatment for cataracts is cataract surgery to remove the opacified lens. We evaluated 2 different types of cataract surgery: (1) extra-capsular cataract extraction with implantation of a posterior chamber intraocular lens (ECCE-PC-IOL); and (2) phacoemulsification with intraocular lens implantation into the posterior chamber (PHACO-PC-IOL).

With ECCE-PC-IOL, the clouded lens and the front portion of the capsule are removed and then replaced with an artificial intraocular lens. PHACO-PC-IOL is a small-incision, sutureless extra-capsular surgery involving the use of an oscillating needle to emulsify the lens nucleus followed by an automated irrigation system to aspirate the lens material from the eye.

Both interventions were assessed at three target coverage levels: 50%, 80%, and 95%, for a total of six separate intervention analyses.

*Estimation of benefits*

We modeled cataracts using the standardized WHO-CHOICE outcomes model, distinguishing susceptibles (those without cataract blindness); cases (those with cataract blindness); and death. Estimates of current incidence and prevalence were based on regional estimates derived from the Global Burden of Disease analysis. Prevalence estimates by age and sex are shown in Table A8.

**Table A8: Prevalence of cataract blindness by age and sex (rates per 1000 population)**

| Age group (years) | Prevalence, male | Prevalence, female |
|---|---|---|
| 0-4 | 0.0 | 0.0 |
| 5-14 | 0.0 | 0.0 |
| 15-29 | 0.0 | 0.0 |
| 30-44 | 1.0 | 0.3 |
| 45-59 | 3.7 | 3.0 |
| 60-69 | 8.2 | 9.4 |
| 70-79 | 12.7 | 16.2 |
| 80+ | 18.1 | 24.1 |

Effectiveness of treatment was modeled using the remission rate; those who are blind bilaterally due to cataracts and whose sight is restored in at least one eye are moved in the model from being ‘cases’ to being ‘susceptibles’ via the remission rate. The null scenario was derived by setting the remission rate in the model to 0 to reflect the absence of cataract surgery. Health-state valuations were derived from the Global Burden of Disease study.

Intervention effectiveness estimates were based on a review of clinical studies as well as the advice of WHO panel experts who assessed the real world effect of cataract surgery, including both surgical effectiveness and patient compliance. Surgical effectiveness estimates for extra-capsular surgery was estimated to be 90% based on a previous study in India.[29] Surgical effectiveness for PHACO was estimated at 96%, based on a previous study in Malaysia.[30] These estimates reflect adjustments for reduced effectiveness due to complications of surgery.

*Estimation of Costs*

Key categories of patient costs associated with delivering the interventions in this analysis included hospital and health centre visits, lab and diagnostic tests, drugs, and surgical procedures. Costs for inpatient and outpatient visits were estimated using standardized WHO-CHOICE unit costs for Mexico (Annex Table). Quantity assumptions were taken from the previous published regional analysis.[28]

Costs of laboratory tests and equipment required for surgery were derived from review of the literature, summarized in Table A9. Costing of PHACO surgery was based on studies comparing PHACO with ECCE and other surgery types.[31 32]

**Table A9: Surgery costs for cataracts (I $)**

| Intervention[a] | Price (procedure alone) | Price (total[b]) |
|---|---|---|
| ECCE-PC-IOL Surgery | 29 | 148 |
| PHACO-PC-IOL Surgery | 38 | 156 |

a. Costs apply across all coverage rates
b. Includes hospital visits and bed days, lab and diagnostic tests, and equipment costs

## Breast cancer

For our analysis of breast cancer interventions in Mexico, we borrowed a number of key assumptions pertaining to the definition of interventions and resource requirements for these interventions from a published WHO-CHOICE analysis,[33] but we developed a more detailed natural history model of breast cancer progression.

*Definition of interventions*

Following the previous regional analysis,[33] we evaluated 6 interventions for treatment and screening for breast cancer: (1) treatment for patients with Stage I breast cancer; (2) treatment for patients with Stage II breast cancer; (3) treatment for patients with Stage III breast cancer; (4) treatment for patients with Stage IV breast cancer; (5) treatment for patients with all stages of breast cancer; and (6) treatment for patients with all stages of breast cancer plus routine population screening. While our primary focus was on comparing treatment (at all stages), with or without the addition of screening, we included stage-specific treatment analyses in order to illuminate the contributions of different components to the overall treatment results.

Definitions of treatment interventions followed those in the previous analysis, which were based on clinical practice guidelines. Treatment for Stage I was defined as lumpectomy with axillary dissection supplemented by radiotherapy, plus endocrine therapy for eligible patients. Treatment for Stage II was defined as lumpectomy with axillary dissection supplemented by radiotherapy, plus endocrine therapy for eligible patients. Treatment for Stage III was defined as neoadjuvant chemotherapy followed by mastectomy with axillary dissection supplemented by radiotherapy, plus endocrine therapy for eligible patients. Treatment for Stage IV was defined as systemic chemotherapy, supplemented with endocrine therapy for eligible patients.

The screening strategy was defined based on the current norm in Mexico. Screening included annual clinical breast examinations for all patients over 25, annual mammogram for patients over 50 (plus high-risk patients over 40), and biennial mammogram for normal-risk patients between 40 and 49 years.

*Estimation of benefits*

We developed a Markov simulation model of breast cancer incidence, progression, detection and mortality, and we calibrated the model to match available epidemiologic information from Mexico. The model distinguishes between breast cancer Stages I, II, III and IV, and further divides each stage into undetected and detected cases. Apart from the additional complexity in the structure of the disease model, compared to the standard five-state model used in the WHO-CHOICE analyses, the breast cancer analysis followed the approach and general methodology used in WHO-CHOICE.

Estimates of current incidence and prevalence were derived from the Global Burden of Disease analysis for Mexico. Table A10 reports on incidence and prevalence by age.

**Table A10: Incidence and prevalence of breast cancer by age (rates per 1000 population)**

| Age group (years) | Incidence | Prevalence |
|---|---|---|
| 0-4 | 0.0 | 0.0 |
| 5-14 | 0.0 | 0.0 |
| 15-29 | 1.2 | 6.7 |
| 30-44 | 23.7 | 141.9 |
| 45-59 | 50.0 | 284.6 |
| 60-69 | 53.1 | 240.8 |
| 70-79 | 66.3 | 227.5 |
| 80+ | 73.5 | 168.0 |

Probabilities of progressing from one stage to the next, and from Stage IV to death for undetected breast cancer cases were estimated from the literature, drawing in large part on published and unpublished reports from the collaborative CISNET modeling program.[34] In the absence of screening, we assumed that cases would be detected based on stage-specific probabilities of clinical surfacing. Health-state valuations were derived from the Global Burden of Disease study.

We modeled the effectiveness of treatment interventions in terms of changes in survivorship, based on data from the National Cancer Data Base in the United States.[35] The effectiveness of screening was modeled by increasing the rate of transitions from undetected to detected cancer, based the characteristics of the screening mode used for a particular target population, and assuming adherence to the screening norm. Table A11 reports the values used for key parameters relating to intervention effectiveness.

**Table A11: Intervention effectiveness inputs for breast cancer**

| Parameter | Value | Sources |
|---|---|---|
| *Case fatality with treatment* (per person per year) | | 35 |
| Stage I | 0.013 | |
| Stage II | 0.042 | |
| Stage III | 0.102 | |
| Stage IV | 0.266 | |
| *Test characteristics* | | 36-42 |
| Clinical breast exam sensitivity | 0.54 | |
| Mammogram sensitivity | 0.71 | |

*Estimation of costs*

Key categories of patient costs associated with delivering the interventions in this analysis included hospital bed days, drugs, treatment procedures, and diagnostic tests. The population screening intervention also included program costs for central administration.

Costs for inpatient and outpatient visits were estimated using standardized WHO-CHOICE unit costs for Mexico (Annex Table). We derived quantity assumptions based on the previous regional CHOICE study on breast cancer.[33] Prices for specific procedures were estimated using the standardized WHO-CHOICE approach to economic costing, and quantities of resource inputs were based on practice guidelines (Table A12).

**Table A12: Prices (I $) and quantity assumptions for major cost categories for breast cancer**

| Category / resource item | Cost per unit | Quantity | Fraction of relevant population incurring cost |
|---|---|---|---|
| *Diagnosis* | | | |
| Bilateral mammography | 28 | Per screening guideline | |
| Biopsy | 33 | Per screening guideline | |
| *Treatment, Stage I or Stage II* | | | |
| Lumpectomy | 183 | 1 | 100% |
| Radiotherapy | 93 | 25 | 100% |

| | | | |
|---|---|---|---|
| Endocrine therapy | 0.25 | 365 | 50% |
| *Treatment, Stage III* | | | |
| Neoadjuvant chemotherapy | 175 | 4 | 100% |
| Mastectomy | 186 | 1 | 100% |
| Radiotherapy | 93 | 25 | 100% |
| Endocrine therapy | 0.25 | 365 | 50% |
| *Treatment, Stage IV* | | | |
| Neoadjuvant chemotherapy | 175 | 4 | 100% |
| Endocrine therapy | 0.25 | 365 | 50% |
| *Follow-up* | | | |
| Bilateral mammography | 28 | 2/1[a] | 100% |
| Pelvic exam | 8 | 2 | 50% |

a. For follow-up, 2 mammograms are included in years 1-5, and 1 mammogram in years 6-10.

## Cervical cancer

At the time of this study, no regional WHO-CHOICE analyses or templates were available for cervical cancer, so we developed the analyses specifically for Mexico using the general approach prescribed in the WHO-CHOICE framework.

*Definition of interventions*

We evaluated 6 interventions for treatment and prevention of cervical cancer: (1) treatment for patients with cervical intraepithelial neoplasia grade 2/3 (CIN 2/3); (2) treatment for patients with local invasive cancer; (3) treatment for patients with regional invasive cancer; (4) treatment for patients with distant invasive cancer; (5) treatment for patients with CIN 2/3 and all stages of invasive cervical cancer; and (6) treatment for patients with CIN 2/3 and all stages of invasive cervical cancer, plus routine population screening. As in the breast cancer analysis, the primary intent of examining treatment at specific stages was to provide a better understanding of the relative contributions of different components to the overall costs and benefits of treatment.

Treatment for patients with CIN 2/3 was defined as loop electrical excision procedure or cryotherapy. Treatment for patients with local invasive cancer was defined as hysterectomy and radiotherapy. Treatment for patients with regional invasive cancer was defined as radiotherapy and cisplatin-based chemotherapy. Treatment for patients with distant invasive cancer was defined as chemotherapy (combination 5-FU and cisplatin).

The screening strategy was defined based on the current norm in Mexico. Screening consisted of a Pap smear and a liquid-based cytology (LBC) test. Women with atypical squamous cells of undetermined significance (ASC-US) were managed using reflex human papillomavirus (HPV) DNA testing and followed-up with colposcopy if necessary. Cytology results including high-grade lesions (ASC-H), low-grade squamous intraepithelial lesions (LSIL), and high-grade squamous intraepithelial lesions (HSIL) moved directly to colposcopy and a follow-up biopsy if necessary.

*Estimation of benefits*

We developed a population-based simulation model of cervical cancer incidence, progression, detection and mortality. The model includes precancerous lesions defined as CIN 2/3, and stages of invasive cervical cancer based on the US National Cancer Institute's Surveillance, Epidemiology, and End-Results Program (local, regional and distant cancer). The model further divides each stage into undetected and detected cases. Apart from the additional complexity in the structure of the disease model used for cervical cancer, compared to the standard five-state model used in the WHO-CHOICE analyses, the cervical cancer analysis followed the general WHO-CHOICE approach.

Estimates of current incidence and prevalence were derived from the Global Burden of Disease analysis for Mexico. Table A13 reports on incidence and prevalence by age.

**Table A13: Incidence and prevalence of cervical cancer by age (rates per 100,000 population)**

| Age group (years) | Incidence | Prevalence |
|---|---|---|
| 0-4 | 0 | 0 |
| 5-14 | 0 | 0 |
| 15-29 | 81 | 45 |
| 30-44 | 592 | 313 |
| 45-59 | 1262 | 655 |
| 60+ | 717 | 461 |

All other model parameters including rates of progression, remission, case fatality, health state valuations, and test characteristics were obtained from a previously published and validated model of cervical cancer.[43]

In the absence of screening, we assumed that cases would be detected based on stage-specific probabilities of clinical surfacing. We modeled the effectiveness of treatment interventions in terms of changes in survivorship for patients in different stages of cancer, and increases in regression from pre-cancerous lesions to the 'well' state. The effectiveness of screening was modeled by increasing the rate of transition from undetected to detected cancer, based the test characteristics of the screening algorithm. Table A14 reports the values used for key parameters relating to intervention effectiveness.

**Table A14: Intervention effectiveness inputs for cervical cancer**

| Parameter | Value | Sources |
|---|---|---|
| *Case fatality with treatment* (per person per year) | | 43-45 |
| Local | 0.030 | |
| Regional | 0.169 | |
| Distant | 0.441 | |
| *Test characteristics* | | 43 46-51 |
| Cytology sensitivity | 0.600 | |
| Cytology specificity | 0.950 | |
| HPV probe assay sensitivity | 0.840 | |
| HPV probe assay specificity | 0.880 | |

### *Estimation of costs*

Key categories of patient costs associated with delivering the interventions in this analysis included hospital bed days, drugs, treatment procedures, and diagnostic tests. The population screening intervention also included program costs for central administration.

Costs for inpatient and outpatient visits were estimated using standardized WHO-CHOICE unit costs for Mexico (Annex Table). We derived quantity assumptions based on previously published studies, and modeled treatment protocols after the guidelines from the American Cancer Society and previous cost-effectiveness studies.[52-54] Prices for specific procedures were estimated using the standardized WHO-CHOICE approach to economic costing, supplemented with information from the *Instituto Nacional de Cancerología* (InCAN) and reported costs from MEXFAM, a nongovernmental organization involved in reproductive health care services[55] (Table A15). Treatment costs were applied to new cases, with follow-up costs applied to all prevalent cases.

**Table A15: Prices (I $) and quantity assumptions for major cost categories for cervical cancer**

| Category / resource item | Cost per unit | Source | Quantity | Fraction of relevant population incurring cost |
|---|---|---|---|---|
| *Diagnosis* | | | | |
| Conventional cervical cytology | 30 | InCAN | Once every three years, annually for all cancer cases | |
| HPV DNA test | 30 | InCAN | 1 | 0.86% |
| Co-collection fee with conventional cytology | 2.6 | InCAN | 1 | 100% |
| Colposcopy and biopsy | 74 | InCAN | 1 | 0.98% |

| | | | | |
|---|---|---|---|---|
| Colposcopy alone | 48 | InCAN | 1 | 0.98% |
| *Precancer treatment* | | | | |
| LEEP | 258 | MEXFAM | 1 | 64% |
| Cryotherapy | 178 | MEXFAM | 1 | 36% |
| *Local treatment* | | | | |
| Hysterectomy | 383 | WHO-CHOICE | 1 | 65% |
| Radiotherapy | 93 | WHO-CHOICE | 46 | 44% |
| Cisplatin-base chemotherapy | 94 | WHO-CHOICE | 5 | 7% |
| *Regional treatment* | | | | |
| Hysterectomy | 383 | WHO-CHOICE | 1 | 10% |
| Radiotherapy | 93 | WHO-CHOICE | 46 | 93% |
| Cisplatin-base chemotherapy | 94 | WHO-CHOICE | 5 | 29% |
| *Distant treatment* | | | | |
| Hysterectomy | 383 | WHO-CHOICE | 1 | 6% |
| Radiotherapy | 93 | WHO-CHOICE | 46 | 72% |
| Chemotherapy (combination 5-FU / cisplatin) | 353 | WHO-CHOICE | 2 | 43% |
| *Follow-up* | | | | |
| Conventional cervical cytology | 30 | InCAN | 1st year: every 3 months | |
| Pelvic exam | 8 | WHO-CHOICE | 2nd year: every 4 months | |
| Chest x-ray | 17 | WHO-CHOICE | 3rd year: every 6 months | |
| | | | 4th and after: annually | |

## Chronic obstructive pulmonary disease

At the time of this study, no regional WHO-CHOICE analyses or templates were available for chronic obstructive pulmonary disease (COPD), so we developed the analyses specifically for Mexico using the generic tools in the WHO-CHOICE framework.

*Definition of interventions*

Current interventions for COPD are aimed at slowing the progression of lung function decline associated with the disease. We evaluated 5 main interventions for treatment of COPD: (1) intensive smoking cessation program for those diagnosed with COPD; (2) influenza vaccine for COPD patients 65 years and older; (3) inhaled bronchodilator for stage II COPD patients; (4) inhaled bronchodilator and corticosteroid for stage III and IV COPD patients; (5) long-term oxygen therapy (in addition to bronchodilator and corticosteroid) for stage IV COPD; and (6) treatment of severe COPD exacerbations. Disease staging was based on Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria.[56]

*Estimation of benefits*

We modeled COPD using the standardized WHO-CHOICE outcomes model, including the states of susceptible (those not having COPD); case (COPD) and death. Estimates of current incidence, prevalence and case-fatality were derived from the Global Burden of Disease analyses for Mexico. Prevalence rates by age and sex are shown in Table A16. Remission rates were assumed to be zero. Health-state valuations were based on the Global Burden of Disease study.

**Table A16: Prevalence of COPD by age and sex (rates per 1000 population)**

| Age group (years) | Prevalence, male | Prevalence, female |
|---|---|---|
| 0-4 | 0.0 | 0.0 |
| 5-14 | 0.0 | 0.0 |
| 15-29 | 0.1 | 0.1 |
| 30-44 | 4.3 | 5.7 |
| 45-59 | 19.9 | 17.2 |
| 60-69 | 47.2 | 36.2 |
| 70-79 | 98.0 | 71.3 |
| 80+ | 163.3 | 122.7 |

Intervention effectiveness was derived from an array of clinical trial and meta-analytic studies (Table A17). For smoking cessation, we note that while the majority of COPD cases are attributable to smoking, many of those who develop COPD do not continue to smoke or previously quit smoking. We accounted for this by scaling the population-level impact of the smoking cessation program by an estimate of smoking prevalence among those already diagnosed with COPD in Mexico. No studies were found that assessed improvements in health state valuations through COPD interventions; thus, we assumed a modest impact on disability for several of the interventions in order to capture improvements in breathing and reductions in frequency of exacerbations, as reported in the literature.

**Table A17: Intervention effectiveness inputs for COPD**

| Intervention / outcome | Efficacy | Sources |
|---|---|---|
| Smoking cessation for COPD patients | | |
| Case-fatality | -15% | [57] |
| Disability | -10% | assumption |

| | | |
|---|---|---|
| Influenza vaccine for COPD patients | | |
| Case-fatality | -12% | [58] |
| Inhaled bronchodilator COPD stage II | | |
| Disability | -10% | assumption |
| Inhaled bronchodilator and corticosteroid COPD stage III and IV | | |
| Case-fatality | -25% | [59 60] |
| Disability | -10% | assumption |
| Long-term oxygen therapy COPD stage IV | | |
| Case-fatality | -50% | [61] |
| Disability | -10% | assumption |
| Treatment for severe exacerbations | | |
| Case-fatality | -6% | [62-64] |
| Disability | -1% | assumption |

*Estimation of costs*

Key categories of patient costs associated with delivering the interventions in this analysis included hospital bed days, drugs and diagnostic tests. The smoking cessation intervention also included program and training costs required for educating doctors and implementing intensive group therapy sessions.

Costs for inpatient and outpatient visits were estimated using standardized WHO-CHOICE unit costs for Mexico (Annex Table), and we derived quantity assumptions based on a review of existing studies (Table A18).

**Table A18: Annual quantities of inpatient bed-days and outpatient visits for COPD**

| **Intervention / outcome** | **Hospital bed-days** | **Outpatient visits** |
|---|---|---|
| Smoking cessation for COPD patients | | 3[b] |
| Influenza vaccine for COPD patients | | 1 |
| Inhaled bronchodilator COPD stage II | | 4.8[c] |
| Inhaled bronchodilator and corticosteroid COPD stage III and IV | | 6.7[c] |
| Long-term oxygen therapy COPD stage IV | | 6.7[c] |
| Treatment for severe exacerbations | 11.9[a] | 2.3[b] |

a. assumed to be 11 days secondary level and 0.9 days ICU[65]
b. Source: [66]
c. Source: [67]

Prices and quantities for medications and diagnostic tests were taken from the literature (Table A19). It should be noted here that we included laboratory test costs for diagnosis in all interventions (which we assumed to be spirometry testing every two years for each case and one chest radiograph upon initial diagnosis).

**Table A19: Prices (I $) and quantity assumptions for major cost categories for COPD**

| Intervention / resource item | Price | Unit | Annual quantity | Population |
|---|---|---|---|---|
| *Smoking cessation for COPD patients* | | | | |
| Nicotine gum | 0.30 | Per piece | 1,405 | Assumed 50% of smoking cessation patients use 7.7 pieces per day for six months[68], and 30% of patients still smoke.[69] |
| *Influenza vaccine for COPD patients* | | | | |
| Inactivated vaccine | 4.37 | Per injection | 1 | Given to COPD patients 65 years and older |
| *Inhaled bronchodilator COPD stage II* | | | | |
| Salbutamol | 2.53 | 20 mg | 3 | Patients stage II (29% of cases)[a] |
| Tiotropium | 4.33 | 18 mcg | 365 | |
| *Inhaled bronchodilator and corticosteroid COPD stage III and IV* | | | | |
| Salbutamol | 2.53 | 20 mg | 3 | Patients stage III and IV (7% of cases)[a] |
| Tiotropium | 4.33 | 18 mcg | 365 | |
| Fluticasone propionate | 12.47 | 5.1 mg | 12 | |
| *Long-term oxygen therapy COPD stage IV* | | | | |
| Salbutamol | 2.53 | 20 mg | 3 | Patients stage IV (2% of cases)[a] |
| Tiotropium | 4.33 | 18 mcg | 365 | |
| Fluticasone propionate | 12.47 | 5.1 mg | 12 | |
| Oxygen | 390.46 | for 1 mo. | 12 | |
| *Treatment for severe exacerbations* | | | | |
| Salbutamol | 2.53 | 20 mg | 14 | Assumed 6% of patients have 1 severe exacerbation per year[b] |
| Tiotropium | 4.33 | 18 mcg | 14 | |
| Fluticasone propionate | 12.47 | 5.1g | 1 | |
| Amoxacillan | 0.10 | 500 mg | 30 | |
| *Diagnostic tests* | | | | |
| Spirometry every 2 years | 15.71 | Per test | | All interventions except treatment of severe exacerbations |
| Chest radiograph | 29.26 | Per x-ray | | Once per individual, all interventions |
| Arterial blood gas | 2.62 | Per test | | Every two years for long-term oxygen therapy; once per individual for severe exacerbations |

a. Distribution of cases across COPD stages from PLATINO study[69]
b. Calculations from[69]

## Cardiovascular disease

Analyses of the cost-effectiveness of interventions for cardiovascular disease (CVD) in Mexico were based on a previously published regional WHO-CHOICE analysis of primary prevention interventions,[70] as well as not-yet-published tools for analysis of treatment and secondary prevention made available by WHO-CHOICE collaborators. The latter have been formalized subsequently in the current regional analysis for CVD.[71]

*Definition of interventions*

We evaluated 12 main interventions for primary prevention of CVD: (1) voluntary decrease of salt in processed foods plus appropriate labeling through cooperation of food manufacturers with government; (2) legislation to decrease salt in processed foods with appropriate labeling and enforcement; (3) mass media health education for cholesterol reduction; (4) hypertension lowering drugs (beta blockers) plus lifestyle modification education, delivered by physicians to individuals with systolic blood pressure (SBP) > 140; (5) hypertension lowering drugs plus lifestyle modification education, delivered by physicians to individuals with SBP > 160; (6) statin plus lifestyle modification, delivered by physicians to individuals with serum cholesterol concentration > 220 mg/dl (> 5.7 mmol/l); (7) statin plus lifestyle modification, delivered by physicians to individuals with serum cholesterol concentration > 240 mg/dl (> 6.2 mmol/l); (8) treatment with beta blocker, statin and aspirin, for individuals with absolute risk of cardiovascular event of 5% in 10 years (5% TRF threshold); (9) treatment with beta blocker, statin and aspirin, 15% TRF threshold; (10) treatment with beta blocker, statin and aspirin, 25% TRF threshold; (11) treatment with beta blocker, statin and aspirin, 35% TRF threshold; (12) combination prevention, including all elements of interventions 4 and 6.

There are two major categories of prevention interventions: non-personal and personal interventions. Non-personal interventions (interventions 1 to 3 above) include health education through mass media programs, legislation or voluntary agreements with the food industry. Personal health-service interventions (Interventions 4 to 12 above) include detection and treatment of high-risk individuals based on blood pressure, cholesterol and computed risk thresholds (the absolute risk approach). The absolute risk approach estimates the combined risk of a cardiovascular event over the next decade above a given threshold, based upon relative risk estimates of modeled risk factors.

We evaluated 19 main interventions for treatment and secondary prevention of CVD. Among this set, 10 interventions focused on acute myocardial infarction (MI) or post-acute ischemic heart disease: (1) aspirin (acute MI); (2) aspirin (post-acute IHD); (3) angiotensin converting enzyme (ACE) inhibitor (acute MI); (4) ACE inhibitor (post-acute IHD); (5) beta blocker (acute MI); (6) beta blocker (post-acute IHD); (7) statin (post-acute IHD); (8) thrombolysis with streptokinase (STK); (9) primary percutaneous transluminal coronary angioplasty (PTCA); and (10) cardiac rehabilitation.

An additional 9 interventions focused on stroke or congestive heart failure (CHF): (11) aspirin (acute ischemic stroke); (12) aspirin (post-acute ischemic stroke); (13) statin (post-acute ischemic stroke); (14) ACE-inhibitor + diuretic (post-stroke); (15) organized stroke unit care; (16) diuretics (CHF); (17) ACE inhibitors (CHF); (18) beta blockers (CHF); (19) exercise training (CHF).

Finally, we considered 11 combination interventions: (20) acute MI treatment (interventions 1+3+5+8); (21) secondary prevention following acute MI (interventions 2+4+6+7); (22) secondary prevention following stroke (interventions 12+13+14); (23) secondary prevention following CHF (interventions 16+17+18+19); (24) statin for secondary prevention following MI and stroke (interventions 7+13); (25) aspirin + beta blocker + statin for secondary prevention following MI or stroke (interventions 2+6+7+12+13); (26) aspirin + beta blocker + ACE inhibitor + PTCA (interventions 1+3+5+9); (27) aspirin + PTCA (interventions 1+9); (28) aspirin + STK (interventions 1+8); (29) aspirin + beta blocker + statin following MI (interventions 2+6+7); (30) aspirin + beta blocker following MI (intervention 2+6).

*Estimation of benefits*

The CVD analysis used the standard WHO-CHOICE state-transition population model (PopMod). Five states were modeled, including the joint disease state, representing the simultaneous presence of both IHD and stroke. In order to account for the relative prevalence of angina and CHF within IHD, an additional modeling tool (MiniMod) was used to determine a weighted disability weight for IHD. The CVD model also took into account an elevated risk of acute MI in those with a previous stroke, and vice versa.

As case-fatality rates from both acute MI and stroke are significantly higher within the first 28 days after the event, deaths from these two diseases were modeled separately based on whether they occurred within the first 28 days (modeled along with background mortality) or whether they occurred after the first 28 days (modeled as fatality hazards from the disease states). The impact of interventions in reducing short-term (28-day) and long-term (>28-day) case-fatality from IHD and stroke were estimated using out-of-hospital case fatality rates derived from the MONICA and GBD studies. The model did not include emergency services in this set of interventions, and thus the out-of-hospital case fatality remained unaffected.

The null scenario was defined as the currently observed incidence and prevalence rates with higher short and long-term in-hospital case fatality rates in the absence of current preventive interventions. The model did not remove the effects of currently implemented interventions on out-of-hospital case-fatality rates in the null scenario. Key incidence estimates are summarized in Table A20.

**Table A20: Epidemiologic estimates for analysis of cardiovascular disease interventions, by age and sex (rates per 1000 population)**

| | Age group (years) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Disease indicator** | **0-4** | **5-14** | **15-29** | **30-44** | **45-59** | **60-69** | **70-79** | **80+** |
| Incidence of acute myocardial infarction | | | | | | | | |
| Male | 0.0 | 0.0 | 0.0 | 0.7 | 4.3 | 9.6 | 13.1 | 17.8 |
| Female | 0.0 | 0.0 | 0.0 | 0.4 | 2.3 | 6.2 | 9.2 | 15.2 |
| Incidence of first stroke | | | | | | | | |
| Male | 0.0 | 0.0 | 0.0 | 0.2 | 1.2 | 4.4 | 8.6 | 16.0 |
| Female | 0.0 | 0.0 | 0.0 | 0.2 | 0.9 | 3.3 | 7.0 | 15.5 |

Intervention effectiveness was determined in WHO-CHOICE regional analyses through systematic review of randomized trials where possible, or meta-analyses. Based on evidence of large cohort studies in diverse populations, joint interventions were assumed to have multiplicative effects. Side-effects relating to bleeding associated with the use of aspirin were included in the analyses. Absent local evidence on treatment adherence, we adopted assumptions from the regional anlaysis. Current coverage rates for hypertension-lowering drugs were estimated from the 2000 *Encuesta Nacional de Salud* (ENSA 2000). Primary prevention intervention assumptions are detailed in Table A21.

**Table A21: Intervention effectiveness inputs, primary prevention interventions for CVD**

| Intervention | Outcome | Effect | Sources |
|---|---|---|---|
| Voluntary cooperation of food manufacturers with government to decrease salt in processed foods, plus appropriate labeling | Total dietary salt intake | -15% | [70 72] |
| Legislation to decrease salt content of processed foods, plus appropriate labeling and | Total dietary salt intake | -30% | [70 73] |

| | | | |
|---|---|---|---|
| enforcement | | | |
| Health education through mass media to reduce cholesterol | Total blood cholesterol | -2% | [70 74] |
| Hypertension-lowering drug treatment and education on lifestyle modification including dietary advice | Difference between actual SBP and 115 mmHg | -33% | [70 75-90] |
| Cholesterol-lowering drug treatment (statins) and education on lifestyle modification including dietary advice | Total blood cholesterol | -20% | [70 91] |
| Anti-platelet drug treatment (aspirin) | Absolute risk of CVD | -20% | [70 92] |

Major CVD risk factor prevalence including systolic blood pressure, blood cholesterol level, BMI and smoking were taken from ENSA 2000. AMR-B data for daily salt intake were used as a proxy for Mexico due to a lack of Mexico-specific data.

CVD deaths were obtained from the Mexican vital registration database after adjustments to account for all-cause garbage codes, CVD-specific garbage codes and miscoding of IHD and stroke deaths to diabetes.[93 94]

Hospital admissions databases from the Ministry of Health and IMSS were analyzed to obtain incidence of 28-day MI (ICD-10 I21) survivors and in-hospital case-fatality rates. To account for incident MI cases occurring outside of the Ministry of Health or IMSS hospitals, a scaling factor was constructed by comparing in-hospital acute MI deaths to acute MI deaths in the 2004 multiple-cause-of-death (MCD) vital registration database coded as having occurred in either an IMSS or a Ministry of Health medical facility. This scaling factor was then used to inflate up MI incidence rates from the hospital admissions data. AMR-B out-of-hospital case fatality rates were used as a proxy for Mexican values when calculating the incidence of first-ever acute MI. Relative risks of IHD mortality were taken from the Danish MONICA study.[95] These epidemiologic estimates were input into the WHO-CHOICE software, DisMod, in order to ensure the internal consistency of our estimates. The output epidemiology from DisMod was then used in the subsequent CVD analyses.

Mortality rates from all stroke (I60 to I69) were obtained from the 2004 MCD vital registry. Incidence rates of first-ever stroke (I60 to I64) were estimated based on a scaling factor constructed from the AMR-B incidence-to-mortality ratio for stroke. The Ministry of Health and IMSS hospital databases were used to estimate in-hospital case fatality rates for both acute MI and stroke.

The first step in modeling the population health effects of each primary prevention intervention was to simulate a population by age and sex with the observed distribution of baseline values for cardiovascular risk factors. Population-level cardiovascular risk was then recalculated after applying the change in risk factor values implied by the effectiveness estimates for each intervention. Reductions in systolic blood pressure were predicted from changes in salt intake, following the previously published regional analysis.[70] Relative risks of cardiovascular disease events for a unit change in risk factor (systolic blood pressure, total blood cholesterol, body mass index, and smoking prevalence) were also adopted from the previous analysis.

Population health effects of the secondary prevention interventions were obtained directly from the cardiovascular mortality rate reductions achieved from each intervention, shown in Table A22. Efficacy estimates were obtained from the literature. Coverage rates of percutaneous transluminal coronary angioplasty (PTCA) (ICD-9-CM 36.01 to 36.09) and injection of a thrombolytic agent (99.10) were calculated using the Ministry of Health and IMSS databases in addition to 2003 OECD Health Data for Mexico. AMR-B prior coverage rates for all other AMI and stroke treatments (aspirin, beta blocker, ACE inhibitor, statin) were used, due to incomplete coding for these treatments in the hospital admissions databases.

**Table A22: Intervention effectiveness inputs, treatment and secondary prevention interventions for CVD[71]**

| Intervention | Outcome | Risk reduction | Sources |
|---|---|---|---|
| *AMI during acute phase (first 28 days)* | | | |
| Aspirin | 28-day AMI case-fatality | -24% | 92 |
| ACE inhibitors | 28-day AMI case-fatality | -7% | 96 |
| Beta blockers | 28-day AMI case-fatality | -4% | 97 |
| Thrombolysis with streptokinase | 28-day AMI case-fatality | -26% | 98 99 |
| Primary PCTA | 28-day AMI case-fatality | -61% | 98-100 |
| *AMI post-acute phase (after 28 days)* | | | |
| Aspirin | Post-28-day MI case-fatality | -15% | 92 |
| ACE inhibitors | Post-28-day MI case-fatality | -21% | 101 |
| Beta blockers | Post-28-day MI case-fatality | -23% | 97 |
| Statin | Post-28-day MI case-fatality | -27% | 102 |
| Cardiac rehabilitation | Post-28-day MI case-fatality | -31% | 103 |
| *Stroke during acute phase (first 28 days)* | | | |
| Aspirin | 28-day ischemic stroke case fatality | -5% | 92 |
| Organized stroke unit care | 28-day stroke case fatality | -14% | 104 |
| *Stroke post-acute phase (after 28 days)* | | | |
| Aspirin | Ischemic stroke (fatal and non-fatal) | -30% | 92 |
| Statin | Ischemic stroke | -28% | 102 |
| ACE-Inhibitor + diuretic | All stroke | -42% | 90 |
| *Congestive Heart Failure* | | | |
| Diuretics | All cause mortality | -75% | 105 |
| ACE inhibitors | All cause mortality | -11% | a |
| Beta blockers | All cause mortality | -22% | 106 |
| Exercise training | All cause mortality | -35% | 107 |

a. Haas et al. 2002, unpublished meta-analysis, as cited in [71]

### *Estimation of costs*

Key categories of patient costs associated with delivering the interventions in this analysis included hospital and health center visits, diagnostic tests, medicines, and surgical procedures. Key categories of program costs included personnel and media.

Costs for inpatient and outpatient visits were estimated using standardized WHO-CHOICE unit costs for Mexico (Annex Table). Quantity assumptions were adopted from the regional WHO-CHOICE analyses.[71]

## Diabetes

At the time of this study, no regional WHO-CHOICE analyses or templates were available for diabetes, so we developed the analyses specifically for Mexico using the general approach prescribed in the WHO-CHOICE framework.

*Definition of interventions*

We considered 4 main interventions for secondary prevention in type 2 diabetes: (1) blood pressure control for diabetic patients with systolic blood pressure higher than 140 mmHg; (2) lipid control for diabetic patients with total cholesterol greater than 200 mg/dL; (3) conventional glycemic control for diabetic patients with $HbA_1c$ greater than 7 percent; (4) intensive glycemic control for diabetic patients with $HbA_1c$ greater than 7 percent.

Blood pressure control was defined as administration of hypertension lowering drugs (beta blockers), plus education on lifestyle modification, delivered by physicians. We modeled this intervention to be consistent with our analyses for primary prevention of cardiovascular disease. Lipid control was defined as administration of statins, plus education on lifestyle modification, delivered by physicians. We modeled this intervention to be consistent with our analyses for primary prevention of cardiovascular disease. Glycemic control interventions were defined based on the intervention and control arms in the United Kingdom Prospective Diabetes Study (UKPDS). Conventional control primarily consisted of diet alone with drug treatment introduced in cases of hyperglycemic symptoms or high fasting plasma glucose. Intensive glycemic control was assumed to follow the randomization in the UKPDS to receive either oral sulphonylureas or insulin.

*Estimation of benefits*

We developed a stochastic microsimulation model of diabetes to capture the long-term health outcomes associated with major risk factors in diabetes patients. The model was developed based on the risk equations in the UKPDS outcomes model,[108] and was used to predict the first occurrence and timing of seven different diabetes-related complications (myocardial infarction, other ischaemic heart disease, stroke, congestive heart failure, lower extremity amputation, renal failure, and blindness in one eye) and death. The model allowed for dependencies between the different disease pathways and for time-varying covariates. The risk equations included age at diagnosis, sex, current smoking, body mass index, $HbA_1c$, systolic blood pressure, and the ratio of total to HDL cholesterol. Population-level estimates of the epidemiology of diabetes in Mexico were based on the Global Burden of Disease analyses for Mexico (Table A23).

**Table A23: Prevalence of diabetes by age and sex (rates per 1000 population)**

| Age group (years) | Prevalence, male | Prevalence, female |
|---|---|---|
| 0-4 | 0.0 | 0.0 |
| 5-14 | 0.1 | 0.1 |
| 15-29 | 0.9 | 1.1 |
| 30-44 | 13.6 | 15.7 |
| 45-59 | 59.8 | 86.7 |
| 60-69 | 85.5 | 155.0 |
| 70-79 | 83.9 | 155.7 |
| 80+ | 95.9 | 159.3 |

The complexity and multiple disease pathways that are relevant in the case of diabetes demanded a more complicated model structure than that afforded by the standard WHO-CHOICE outcomes model. In addition, because of the many individual risk factors that are relevant to diabetes outcomes, a microsimulation model was most appropriate. However, apart from the particular modeling techniques that were used for the analysis, our diabetes analysis was undertaken following the approach and general methodology that applies to all of the standard WHO-CHOICE analyses.

Risk factor distributions in Mexico were estimated based on the baseline *Seguro Popular* survey. While this survey is not representative of the entire population in Mexico, data on blood glucose from ENSANut 2005 were not available for these analyses, and we did not identify any other survey that included all relevant variables needed to estimate the risk equations. We defined the target population for interventions as those with fasting plasma glucose greater than or equal to 126 mg/dL. The survey included direct measurement of casual, rather than fasting, plasma glucose for most respondents, so we predicted fasting measures for those in whom direct observations were not available following the same model used in a companion study on Effective Coverage of the Health System in Mexico 2000-2003. The survey measured total cholesterol but not HDL, so we predicted the ratio of total to HDL cholesterol based on age-specific relationships in the United States NHANES III survey. Observations on $HbA_1c$ were unavailable for a proportion of survey respondents, so we predicted missing values based on age, sex, body mass index, blood pressure and blood glucose.

Case-fatality rates for diabetes complications were defined to be consistent with our analyses of cardiovascular disease interventions and interventions for end-stage renal disease. Health-state valuations for states in the model were derived from published data from the Global Burden of Disease study, the UKPDS and the CDC Diabetes Cost-Effectiveness Group.[109 110]

Effectiveness estimates for blood pressure control and lipid control were defined to be consistent with our analyses of cardiovascular disease interventions (based on systematic reviews in the literature). Effectiveness of glycemic control was estimated based on trial results in the UKPDS, as used in prior cost-effectiveness analyses [109 111] (Table A24).

**Table A24: Intervention effectiveness inputs for diabetes**

| Intervention / outcome | Effect | Notes and sources |
|---|---|---|
| *Blood pressure control* | | |
| Difference between actual SBP and 115 mgHg | -33% | [70 75-90] |
| *Lipid control* | | |
| Ratio of total to HDL cholesterol | -24% | Effect of statins on total:HDL ratio based on 20% reduction in total cholesterol[70 91] combined with 5% increase in HDL. |
| *Glycemic control* (conventional / intensive) | | |
| $HbA_1c$ level | -2.0 / -2.9 | Those on treatment subject to maximum $HbA_1c$ level of 9.0, compared to maximum of 14.0 for those not on treatment.[109 111] |

The simulation model was used to compute the number of events, including deaths, life expectancy, and disability-adjusted life years for the population of patients targeted by each intervention. For each intervention, two simulations were undertaken: one without the intervention and one with the intervention. Differences in outcomes between the null and intervention scenarios were computed by sex and age group.

To be consistent with the approach used in all other analyses, based on the guidelines from WHO-CHOICE, we extrapolated from the outcomes in the simulation model—which generated average outcomes for patients by age and sex—to the entire Mexican target populations, and to the assumed 10-

year duration of therapy, as follows. We assumed that the cumulative target population for a given intervention over the course of the 10-year intervention period would include all eligible prevalent cases in the first year, plus all eligible incident cases in years two through 10. We further assumed that patients who experienced the intervention for a period of less than 10 years would face both costs and health benefits that scaled linearly with the intervention duration. Finally, in order to include the 3% annual discount rate applied in all analyses to both costs and health outcomes, we computed the present value of the cumulative 10-year target population by applying appropriate discount factors to all new treatment-eligible cohorts added after the first year. The final result was a present value cumulative treatment population estimate to which we applied both the age-sex specific DALYs averted per patient, as well as the age-sex specific estimates of average treatment years per new patient to compute costs.

*Estimation of costs*

Key categories of patient costs associated with delivering the interventions in this analysis included health center visits, hospital visits, drugs and laboratory tests. Cost assumptions for blood pressure control and lipid control were defined to be consistent with our analyses of cardiovascular disease interventions.

Prices for inpatient and outpatient visits were estimated using standardized WHO-CHOICE unit costs for Mexico (Annex Table). Quantity assumptions were based on WHO-CHOICE estimates, derived from the literature (Table A25), or from trial protocols in the case of the two interventions for glycemic control.

**Table A25: Annual quantities of inpatient bed-days and outpatient visits for diabetes**

| Intervention / population | Hospital visits | Health center visits |
|---|---|---|
| *Blood pressure control* | | |
| All intervention recipients | 1.5[a] | 4[b] |
| *Lipid control* | | |
| All intervention recipients | 1.5[a] | 4[b] |
| *Glycemic control* (conventional) | | |
| All intervention recipients | 1.5[a] | 4.2[c] |
| *Glycemic control* (intensive) | | |
| All intervention recipients | 1.5[a] | 6.7[c] |

a. Assumed primary level
b. Assumed duration of 10 minutes and coverage of 95%.
c. Assumed duration of 30 minutes and coverage of 95%. Estimates drawn from UKPDS, and computed as weighted average of number of physician visits for patients receiving or not receiving insulin.

Estimates of quantities of other inputs were based on current management guidelines. Prices for drugs were derived from the IMSS price list (Table A26).

**Table A26: Annual prices (I $) for other major cost categories for diabetes**

| Intervention / resource item | Yearly price per patient[a] |
|---|---|
| *Blood pressure control* | |
| Propanolol (Beta blockers) | 15 |
| Hydrochlorotiazide (diuretic) | 20 |
| *Lipid control* | |

| | |
|---|---|
| Pravastatin | 103 |
| *Glycemic control* (conventional) | |
| Glibenclamide | 1.88 |
| Metformin | 2.23 |
| Insulin | 34 |
| $HbA_1c$ tests | 14 |
| Home glucose tests | 95 |
| *Glycemic control* (intensive) | |
| Glibenclamide | 3.87 |
| Metformin | 2.45 |
| Insulin | 80 |
| $HbA_1c$ tests | 14 |
| Home glucose tests | 122 |

a. Yearly prices incorporate coverage levels of 95% and account for the fraction of eligible patients receiving the specific item.

## Annex Tables

Unit costs for hospital bed-days, hospital outpatient visits and health center visits in Mexico (Source: WHO-CHOICE price database)

**Annex Table A. Prices for hospital bed-days and outpatient visits (2005 pesos)**

| Facility type | Unit cost per bed day | Unit cost per visit |
|---|---|---|
| Primary-level hospital: Most basic hospital unit, with few specialties mainly limited to internal medicine, obstetrics-gynecology, pediatrics and general surgery. | 505 | 176 |
| Secondary-level hospital: Clinical services are highly differentiated by function and have five to ten clinical specialties. | 659 | 378 |
| Tertiary-level hospital: Highly specialized staff and equipment. | 900 | 559 |

**Annex Table B. Prices for health center visits (2005 pesos)**

| Population coverage level | Duration of visit | | | | | | |
|---|---|---|---|---|---|---|---|
| | 2 | 10 | 20 | 30 | 40 | 50 | 60 |
| 10% | 63 | 106 | 127 | 140 | 151 | 160 | 167 |
| 20% | 71 | 106 | 127 | 140 | 151 | 160 | 167 |
| 30% | 71 | 106 | 127 | 140 | 151 | 160 | 167 |
| 40% | 71 | 106 | 127 | 140 | 151 | 160 | 167 |
| 50% | 71 | 106 | 127 | 140 | 151 | 160 | 167 |
| 60% | 71 | 106 | 127 | 140 | 151 | 160 | 167 |
| 70% | 71 | 106 | 127 | 140 | 151 | 160 | 167 |
| 80% | 71 | 107 | 127 | 141 | 152 | 161 | 168 |
| 90% | 74 | 112 | 133 | 148 | 159 | 168 | 176 |
| 95% | 79 | 119 | 142 | 157 | 169 | 179 | 187 |
| 100% | 100 | 151 | 180 | 199 | 214 | 227 | 238 |

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